SUPPLEMENTAL MATERIAL

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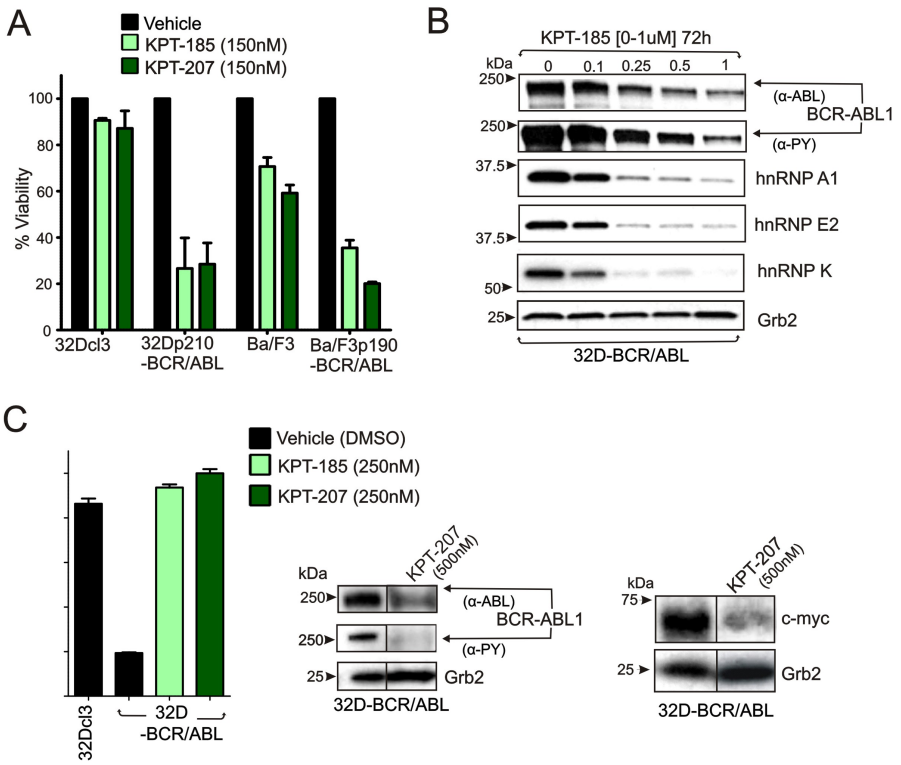
***Cell cultures and primary cells*.** Parental, BCR-ABL1-expressing 32Dcl3 and BaF3 cells were maintained in culture in Iscove's modified Dulbecco's medium (IMDM)/10% FBS/2 mM L-glutamine. $CD34^+$ and $CD34^+/CD19^+$ progenitors were isolated using magnetic activated cell sorting (MACS; Miltenyi Biotec), and CD19-PE/CD34-FITC fluorescence activated cell sorting (FACS Aria II; BD biosciences), respectively. Primary cells were kept in IMDM supplemented with 30% FBS, 2 mM glutamine, rhIL-3 (20 ng/ml), rhIL-6 (20 ng/ml), rhFlt-3 ligand (100 ng/ml), and rhKL (100 ng/ml) (Stem Cell Technologies). Progenitors isolated from ALL patients and the corresponding healthy donor control cells were cultured on irradiated (30γ) hTERT.BMS feeder cells in IMDM supplemented with 30% FBS, 2 mM glutamine, and rhIL-7 (100 ng/ml) and rhSCF (100 ng/ml) (PeproTech). Apoptosis was measured by flow cytometry (LSRII; BD Biosciences) on 7-AAD/Annexin V-FITC-stained cells cultured on immortalized human hTERT.BMS stromal cells to increase viability by mimicking the BM microenvironment[35]. Data were analyzed using FlowJo or Diva FACS software (BD Biosciences). Methylcellulose clonogenic assays were carried out by plating $5x10^3$ $CD34^+$ CML and NBM progenitors in 0.9% MethoCult H4435 (Stem Cell Technologies) with DMSO or KPT-330 at concentrations indicated in results section. Colonies (>20 μm) were scored 14 days later.

Quantitative Real-Time PCR: Total RNA was isolated from $1\text{-}3x10^6$ cells using Trizol (Invitrogen) and cDNA was generated using random hexamer primers and Moloney murine leukemia virus (M-MLV) reverse transcriptase (Invitrogen). Expression of *BCR-ABL1* and *XPO1* were measured as a percentage of 18S RNA levels by SYBR Green Assay (Applied Biosystems). Assays were performed three-times in duplicate using the primers: XPO1(F): 5'-tggagaagtaatgccgttcattg-3'; XPO1(R): 5'-cccacacttgattagggagtagc-3'; BCR-ABL1(F): 5′-cgtccactcagccactggat-3′; BCR-ABL1(R): 5′-ggcttcactcagaccctgagg-3′.

Western blot analysis and subcellular fractionation: $1\text{-}3x10^6$ cells were lysed by freezing/thawing in 250mM Sucrose, 20mM HEPES (pH 7.4), 10mM KCl, 1.5mM MgCl2, 1mM EDTA, 1mM EGTA, 1mM DTT in the presence of protease inhibitor cocktail. Lysates were either clarified by centrifugation and used as whole-cell lysates or centrifuged (720xg; 5 min, 4C) to pellet nuclei. The supernatant was further clarified (16000xg; 20 min, 4C) to isolate the cytoplasmic fraction. After 3X washing in lysis buffer, nuclear pellets were dissolved in Laemmli buffer and subjected to immunoblots.

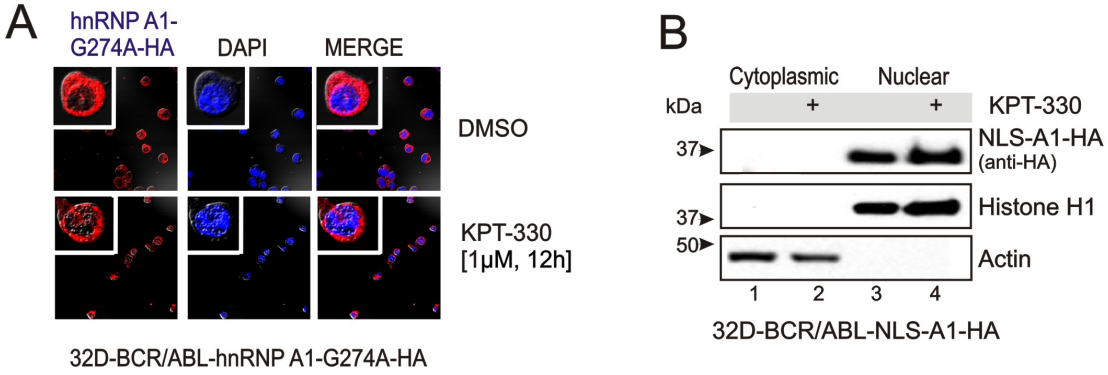
SUPPLEMENTAL FIGURES

Supplemental Figure 1



Supplemental Figure 1. KPT-185 and -207 preferentially kill BCR-ABL1$^+$ cells through reduction of hnRNP proteins and activation of PP2A. (A) Viability of BCR-ABL1-expressing 32Dp210-BCR/ABL myeloid and Ba/F3p190-BCR/ABL lymphoid cells and non-transformed parental cells treated with KPT-185, KPT-207, or vehicle (150nM, 72h). Errors bar are SEM of experiments performed in triplicate. (B) Protein levels of hnRNP A1, hnRNP E2, hnRNP K and BCR-ABL1 activity (anti-PY) and expression (anti-ABL) in KPT-185 (0-1μM, 72h)-treated 32D-BCR/ABL cells. (C) Left Panel: PP2A activity in 32Dcl3, and vehicle- (black bar), KPT-185- (light green bar), and KPT-207- (dark green bar) treated 32D-BCR/ABL cells. PP2A levels were normalized to those of 32Dcl3 cells. Middle and Right Panels: BCR-ABL1 levels (anti-ABL) and activity (anti-PY), and c-Myc expression in KPT-207 (0-1μM, 72h)-treated 32D-BCR/ABL cells.

Supplemental Figure 2



Supplemental Figure 2: KPT-330-mediated interference with hnRNP A1 shuttling is dependent on the integrity of the M9 domain (A) Single channel and merged confocal micrographs of vehicle- and KPT-330 (1μM, 12h)-treated 32D-BCR/ABL cells ectopically expressing the shuttling-deficient cytoplasmic hnRNP A1-G274A-HA cells; cells were stained with anti-HA antibody (left panel; red), DAPI (middle; blue) and merged (right). (B) Ectopic expression of the nuclear-localized shuttling-deficient (NLS-A1-HA) hnRNP A1 mutant protein. Levels were assessed by anti-HA immunoblots in nuclear and cytoplasmic subcellular fractionated extracts from vehicle- and KPT-330-treated (1μM, 12h) 32D-BCR/ABL-NLS-A1-HA cells.